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EXAMINER

LEFFERS JR, GERALD G

ART UNIT PAPER NUMBER

1636

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/808,388

Applicant(s)

MASSAAD ET AL.

Examiner

Gerald G Leffers Jr., PhD

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26-29, 31 and 35-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 48 and 49 is/are allowed.
- 6) ☐ Claim(s) 26-29, 31, 35-39, 41-47 and 50-52 is/are rejected.
- 7) ☒ Claim(s) 40 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 7/11/2001, page 2.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/11/2003 has been entered.

In the response filed on 12/11/2003, applicants' have amended several claims (claims 26-29, 31, 35-42, 45-48 and 50-52) and cancelled several claims (claims 30 and 32-34). Claims 26-29, 31 and 35-52 are pending in the instant application. It is noted that in applicants' response applicants failed to point to where in the specification support exists for the specific new limitations of claim 26, part b. However, upon review of the instant specification, it appears literal support for this set of limitations concerning SEQ ID NO: 5 are found on page 12 of the instant specification. This action is not final.

Information Disclosure Statement

Upon review of the instant application, it is apparent that the final reference of the IDS filed 7/11/2001 was not initialed as considered on the corresponding PTO Form 1449. A corrected copy of this form has been initialed and mailed along with this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1636

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejected claims are directed to a hybrid promoter comprising a peroxisome proliferator activated receptor response element (i.e. a PPAR response element) operatively linked to a “heterologous sequence from a promoter of a IIA-1 nonpancreatic secreted phospholipase A2 (i.e. PLA2s) gene”. The latter limitation can reasonably be interpreted broadly to encompass any dinucleotide sequence present in a PLA2s gene obtained from any source that is operatively linked to a PPAR response element. Some of the dependent claims comprise the limitation that the PPAR element is a “functional variant” of one of SEQ ID NOS: 1-4. This term is not explicitly defined in the specification such that it cannot be read to encompass literally any PPAR response element obtained from any source, a reasonable interpretation in the absence of explicit guidance as to what is not encompassed by the term.

Claims 26-29, 31, 41, 43, 46 and 50-51 are rejected under 35 U.S.C. 102(a) as being anticipated by Couturier et al (J. Biol. Chemistry, August 1999, Vol. 274, No. 33, pages 23085-23093; already of record in prosecution of the instant application, see the entire document). **This is a new rejection necessitated by applicants’ amendment of the claims in the response filed 12/11/2003.**

Couturier et al describe the characterization of the PLA2s gene and those elements that are responsible for regulating transcription of the gene. Couturier et al demonstrate that the rat PLA2s promoter comprises at least one PPAR-binding element with extensive homology with a known PPRA-binding element (e.g. DR1) (e.g. page 23090, column 2, 4th paragraph; Figure 9). Couturier et al teach at least one embodiment where 2 copies of a PPAR element are operatively linked to a thymidine kinase promoter that is further linked to a reporter gene (i.e. a luciferase coding sequence) in a plasmid vector and where reporter gene activation in smooth muscle cells in the presence of IL1B is measured (e.g. Figure 9B). One of skill in the art would necessarily expect that the thymidine kinase promoter taught by Couturier et al would necessarily comprise at least one dinucleotide sequence present in at least one PLA2s gene obtained from at least one source. Therefore, Couturier et al teach a PPAR response element operatively linked to a “heterologous sequence” from a PLA2s gene.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 26-29, 41, 43, 46, 50-51 are rejected under 35 U.S.C. 102(e) as being anticipated by Evans et al (U.S. Patent No. 6,413,994; already of record in the prosecution of the instant

application, see the entire reference). **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 12/11/2003.**

Evans et al teach the use of PPAR γ -binding elements (up to three copies) operatively linked to a reporter gene under control of a thymidine kinase promoter in order to identify compounds that modulate the activity of PPAR γ (e.g. the Abstract, Example 2). The TK promoter would necessarily comprise at least one nucleotide sequence from the PLA2s promoter (i.e. a "heterologous sequence" from a PLA2s promoter) operatively linked to at least one copy of a "functional variant" of a PPAR-binding element. The reporter constructs were subsequently transfected into CV-1 cells and used to screen for PPAR antagonists (e.g. Example 3).

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 26, 29, 41, 43, 46 and 50-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Juge-Aubry, et al (The Journal of Biological Chemistry, Vol. 272, No. 40, pages 25252-25259, October 1997; already of record in the prosecution of the instant application, see the entire reference). **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 12/11/2003.**

Juge-Aubry et al teach the DNA binding properties of PPAR receptor subtypes on various natural PPAR response elements (e.g. the Abstract; Figures 2 and 5). The reference also teaches at least one embodiment where the transcriptional activity of a construct comprising a hybrid PPAR element is operatively linked to a reporter gene is assessed in transfected HepB2 cells (e.g. Figure 6). In the hybrid element, the 5' flanking sequence of DR1 from HMG was linked to the core DR1 sequence of ARE6 (e.g. Figure 5; page 25257, column 2). Such a construction, having a hybrid PPAR element operatively linked to a promoter and reporter coding sequence would necessarily satisfy the limitation of being a part of a "hybrid promoter" comprising a functional PPAR element operatively linked to a "heterologous sequence" from a PLA2s gene.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Juge-Aubry, et al (The Journal of Biological Chemistry, Vol. 272, No. 40, pages 25252-25259, October 1997; already of record in the prosecution of the instant application, see the entire reference). **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 12/11/2003.**

The teachings of Juge-Aubry et al are described above and are applied as before, except: Juge-Aubry et al teach a consensus sequence for PPRE elements derived from 16 sequences obtained from 16 natural sources. The consensus sequence is described by SEQ ID NO: 1 of the instant application. Juge-Aubry et al characterize the ability of different PPAR/RXR complexes to bind nucleic acids comprising the natural PPRE sequences (e.g. Figure 3). In their experiments concerning the transcriptional activity of HMG, ARE6 and hybrid HMG/ARE6 elements, the authors assay the transcriptional activity in the presence of compounds (ETYA or BRL) that enhance transcriptional activity (i.e. PPAR activators).

Juge-Aubry et al do not appear to reduce to practice any nucleic acid comprising the consensus sequence (i.e. SEQ ID NO: 1) or to teach a composition comprising the consensus sequence and a PPAR activator.

It would have been obvious to construct and use a nucleic acid sequence comprising the consensus sequence taught by Juge-Aubry in their experiments to determine the binding/functional characteristics of various PPRE elements because Juge-Aubry et al teach it is within the skill of the art to characterize the binding/functional characteristics of such elements (e.g. the artificial hybrid element HMG/ARE6). One would have been motivated to do so in order to further characterize the binding/functional properties of such PPRE elements with regard to what is proposed to be a “consensus” sequence. Absent any evidence to the contrary, there would have been a reasonable expectation of success in constructing and using a nucleic acid comprising the consensus sequence taught by Juge-Aubry et al in the experiments taught by Juge-Aubry et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-29, 31, 35-38, 41-44, 46-47, 50-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections necessitated by applicants' amendment of the claims in the papers filed 12/11/2003.**

Claim 26 is vague and indefinite in that the metes and bounds of the term “heterologous sequence” from part (b) of the claim are unclear. It is unclear as the claim is written whether the term applies to the second part of part (b) where the sequence is a sequence of a PLA2s gene comprising specific portions of SEQ ID NO: 5. It thus remains unclear, for example, if a PLA2s promoter/enhance comprising a PPAR obtained from the PLA2s gene and the PLA2s promoter as well as other regulatory elements (e.g. a Tet operator sequence) would read on the claims. It appears from reading the specification that it may be intended that part (b) specifies that the PLA2s promoter sequences are obtained from a source different from that from which the PPAR element of part (a) is obtained. It would be remedial to amend the claim to clearly indicate that the term “heterologous sequence” applies to the nucleic acid sequence comprising the specified residues of SEQ ID NO: 5.

Claims 37 and 38 are vague and indefinite in that there is no clear and positive prior antecedent basis for the limitation of “said sequence” as there are multiple sequences in the claims upon which claims 37-38 depend.


Conclusion

Claims 26-29, 31 and 35-52 are pending in the instant application, with claims 26-29, 31, 35-39, 41-47 and 50-52 rejected. Claims 48-49 are allowed. Claim 40 is objected to as being dependent upon a rejected claim, but would be allowable if rewritten to include all of the limitations of the claim upon which it is currently dependent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

GERRY LEFFERS
PRIMARY EXAMINER

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